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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,647	07/17/2001	Ramachandran Murali	UPN-3963	3796
7278	7590	03/24/2006	EXAMINER	
DARBY & DARBY P.C. P. O. BOX 5257 NEW YORK, NY 10150-5257			CLOW, LORI A	
			ART UNIT	PAPER NUMBER

1631-

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/720,647

Applicant(s)

MURALI ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 2-5 and 9-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 6-8 and 25-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicants' arguments, filed 19 September 2005, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-31 are currently pending. This application contains claims 2-5 and 9-24 drawn to an invention nonelected with traverse in the reply filed 18 October 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 25 has been amended to recite "wherein identifying the allosteric cavity within the structure of a target protein in step a) comprises using nuclear magnetic resonance, crystal structure analysis, calorimetric values from thermodynamic studies, or computer modeling".

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Applicant points to support for this amendment at page 10, line 18. However, this is not persuasive. The specification, at page 10, line 18, teaches identifying functionally critical sites on a target protein by using these techniques. The specification does not teach using these techniques to identify an allosteric cavity.

Claim 31 recites “wherein the allosteric cavity is identified using nuclear magnetic resonance or crystal structure analysis and further comprises identifying thermal  $\beta$ -factors”.

Applicant points to support for this newly added claim at page 11, lines 3-5. However, this is not persuasive, as lines 3-5 of page 11 state only that the cavity of the target protein may be identified by any of several techniques including crystal structure analysis, NMR, and computer modeling. This does not include thermal  $\beta$ -factors in reference to the allosteric cavity and therefore, this is new matter.

### **Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 6-8, and 26-30 remain rejected under 35 U.S.C. 102(a) as being anticipated by Aghajari et al. (Protein Science (1998) Vol. 7, pages 564-572), for the reasons set forth in the previous Office Action mailed 17 June 2005.

*Response to Applicant's Arguments*

1. Applicant argues that “the present invention is not directed to the well-known technique of allosteric modification”. This is not persuasive, as the claims clearly set forth “a method of identifying a compound that is an allosteric modulator”. Therefore the claims do comprise limitations directed to allosteric modification, as recited in the preamble.

2. Applicant argues that “implicit in the claim language is the concept that, in order to carry out the claimed step of identifying a *candidate* allosteric cavity, such a cavity must not be already known to be an allosteric site of the protein-of-interest (or it would not be a “candidate cavity”)”.

This is not persuasive, as the claims do not recite a step of identifying an *unknown* allosteric cavity. Rather, the claims recite identifying a candidate, as Applicant has pointed out. There is nothing implicit in the word *candidate* that equates its meaning to “unknown”. A candidate is “one likely or suited to undergo or be chosen for something specified” (Merriam-Webster Dictionary, 10<sup>th</sup> Edition, 1999). Therefore, Aghajari does teach the identification of a candidate (i.e. chosen) allosteric cavity, as stated in the previous Office Action.

3. Applicant argues that Aghajari did not discover, and does not disclose, that binding chloride ion or any other cofactor *modulates* enzyme function. Rather it is a condition precedent for enzyme function.

This is not persuasive. Applicant admits that “a chloride ion, which functions as an allosteric co-factor, is required for activity of  $\alpha$ -amylase”. This is clearly modulating enzyme function. The claims are not drawn to “the inhibition of”, for example, or some other mode of activity. The claims merely recite “modulate”, which is defined as “to adjust or keep in proper

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measure or proportion” (Merriam-Webster Dictionary, 10<sup>th</sup> Edition, 1999). Any molecule which “adjusts” the activity, i.e. by turning on activity, is by definition a modulator.

4. Applicant continues the argument with regard to the claims being drawn to “candidate” sites. Applicant states that chloride ion was already known as a necessary cofactor to regulate enzyme function. Applicant outlines the claims in terms of identification of a candidate and the modulation of the target. Applicant states that clearly “this type of identification (in reference to the identification outlined as taught by Aghajari) has nothing to do with identifying a candidate allosteric cavity or identifying compounds that bind in the newly identified allosteric cavity as potential allosteric modulators of a protein, as called for in the present claims”. These arguments are not persuasive, as they are drawn to the same logic as above. Further, the present claims are not drawn to a “newly identified allosteric cavity” or a “potential allosteric modulator”.

For these reasons and those previously set forth, the rejection is maintained.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

### Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

March 20, 2006  
Lori A. Clow, Ph.D.  
Art Unit 1631  
*Lori A. Clow*

MARJORIE A. MORAN  
PRIMARY EXAMINER

*Marjorie A. Moran*  
3/20/06